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L2: Entry 4 of 7 File: USPT Jun 15, 2004

US-PAT-NO: 6749855
DOCUMENT-IDENTIFIER: US 6749855 B2

TITLE: Methods of use of recombinant vasoactive protein from salivary gland of the black fly

DATE-ISSUED: June 15, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Cupp; Mary S.	Auburn	AL		
Ribeiro; Jose M. C.	Rockville	MD		
Cupp; Eddie W.	Auburn	AL		

US-CL-CURRENT: 424/185.1; 514/12

CLAIMS:

That which is claimed is:

1. A method for lowering peripheral vascular resistance in a mammal, said method comprising administering a therapeutically effective amount of a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 2, that increases blood flow whereby the peripheral vascular resistance is lowered.

2. A method for lowering peripheral vascular resistance in a mammal, said method comprising administering a therapeutically effective amount of a polypeptide comprising the mature form of the amino acid sequence of SEQ ID NO:2 that increases blood flow, whereby the peripheral vascular resistance is lowered.

3. The method of claim 1, wherein said polypeptide is produced by recombinant methods.

4. A method for lowering peripheral vascular resistance in a mammal, said method comprising administering a therapeutically effective amount of a polypeptide encoded by a nucleotide sequence comprising the sequence set forth in nucleotides 49 504 of SEQ ID NO:1 that increases blood flow, whereby the peripheral vascular resistance is lowered.

5. The method of claim 1, wherein said step of administering said polypeptide comprises administration by intradermal injection.

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L2: Entry 7 of 7 File: USPT Dec 19, 2000

US-PAT-NO: 6162785
DOCUMENT-IDENTIFIER: US 6162785 A

TITLE: Recombinant vasoactive protein from salivary gland of the black fly

DATE-ISSUED: December 19, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Cupp; Mary S.	Auburn	AL		
Ribeiro; Jose M. C.	Rockville	MD		
Cupp; Eddie W.	Auburn	AL		
Swaim; Steven F.	Auburn	AL		

US-CL-CURRENT: 514/2; 530/350

CLAIMS:

That which is claimed is:

1. A substantially purified polypeptide comprising the amino acid sequence set forth in SEQ ID NO:2.

2. A composition comprising a polypeptide having the amino acid sequence set forth in SEQ ID NO:2 and a pharmaceutically acceptable carrier.

Previous Doc Next Doc Go to Doc#

L2: Entry 6 of 7 File: USPT Dec 31, 2002

US-PAT-NO: 6500420
DOCUMENT-IDENTIFIER: US 6500420 B1

TITLE: Recombinant vasoactive protein from salivary gland of the black fly

DATE-ISSUED: December 31, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Cupp; Mary S.	Auburn	AL		
Ribeiro; Jose M. C.	Rockville	MD		
Cupp; Eddie W.	Auburn	AL		

US-CL-CURRENT: 424/93.2; 435/252.3, 435/253.6, 435/320.1, 435/69.1, 514/12, 530/350, 536/23.5

CLAIMS:

That which is claimed is:

1. An isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1.

2. An isolated nucleic acid molecule encoding the polypeptide of SEQ ID NO:2.

3. The isolated nucleic acid molecule of claim 2, wherein said sequence encodes the mature polypeptide of SEQ ID NO:2.

4. A vector comprising the nucleic acid molecule of claim 1.

5. A host cell comprising the vector of claim 4.

6. A DNA construct comprising the nucleic acid molecule of claim 1 operably linked to a promoter.

7. A host cell comprising the DNA construct of claim 6, wherein said promoter is active in said host cell.

8. A method of producing a polypeptide comprising culturing the host cell of claim 7.

9. The method of claim 8, further comprising isolating the polypeptide from the cell or the cell culture supernatant.

10. A solution comprising a cell culture supernatant of the host cell of claim 7.

11. A cell lysate derived from the host cell of claim 7.

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1: J Surg Res. 2002 Sep;107(1):18-26.

Skin blood flow response in the rat model of wound healing: expression of vasoactive factors.

Rendell MS, Johnson ML, Smith D, Finney D, Capp C, Lammers R, Lancaster S.

The Creighton Diabetes Center, Omaha, Nebraska 68131, USA. rendell@asndi.com

BACKGROUND: Although the microvascular blood flow response to wounding is predominantly vasodilation at skin sites with nutritive capillary perfusion (NUTR), there is a significant vasoconstrictive response at sites with high arteriovenous perfusion (AV). There may be a difference between NUTR and AV sites in the vasoactive factors which mediate the blood flow response to wounding. We measured the levels of mRNA expression of several potential mediators of the blood flow response to assess this possible difference. MATERIALS AND METHODS: We measured skin blood flow at wounds placed at the back, a NUTR site, and at the paw, an AV site, in 12 Wistar Kyoto rats. Measurements were performed at baseline and then at 7 days post wounding. There was a significant increase in blood flow at back wound sites, with a rise from 4.1 +/- 0.3 ml/min/100 g to 9.8 +/- 1.9 ml/min/100 g. At the undisturbed wound perimeter, outside the zone of granulation tissue, flow rose to 7.3 +/- 1.1 ml/min/100 g. At the paw wound site, Day 0 flow was 8.8 +/- 0.8 ml/min/100 g. At 7 days, there was a significant decrease in flow at wound center to 5.5 +/- 0.5 ml/min/100 g. We measured the levels of inducible nitric oxide synthetase (iNOS), endothelin, endothelin receptor, vascular endothelial growth factor (VEGF), and keratinocyte growth factor (KGF) gene mRNAs using reverse transcriptase PCR. RESULTS: There was a 10-fold increase in NOS mRNA in granulation tissue of both wounds on Day 7. There was a lesser but still substantial increase in the wound perimeter tissue. Levels of endothelin mRNA in the wound and wound perimeter were significantly lower at the paw than at the back. At baseline, the level of endothelin receptor B (ETrB) mRNA was greater at the back than at the paw. Wounding resulted in a substantial increase in EtrB mRNA levels in granulation tissue, reaching the same level at the back and paw wounds. There was also a substantial rise in EtrB mRNA levels at the paw wound perimeter, so that there was a reversal of the baseline condition, with paw levels actually surpassing the levels at

the back perimeter. CONCLUSIONS: Thus, we have found significant changes in mediators both of vasoconstriction and vasodilation affecting the healing wound. These changes affect NUTR and AV sites in different ways. These results demonstrate the complexity of the regulatory processes controlling microvascular blood flow in wound healing.

PMID: 12384060 [PubMed - indexed for MEDLINE]

1: Orthopedics. 2000 Jan;23(1):33-6.

Related Articles, Links

Skin blood flow level and stump healing in ischemic amputations.

Avci S, Musdal Y.

Department of Orthopedics, Faith University School of Medicine, Ankara, Turkey.

Skin blood flow was measured with xenon 133-histamine mixture in 20 lower extremities of 18 patients before performing amputations. The amputation levels were chosen according to clinical criteria; 13 below-knee, 3 distal femoral, 1 midfemoral, 2 transmetatarsal, and 1 Syme's amputations were performed. Fourteen stumps had normal healing, 2 had delayed healing, and 3 had necrosis. All of the stumps with normal healing had a skin blood flow >1.76 ml/100 g tissue/minute. Bleeding from the skin also was a good predictor of healing. Skin blood flow measurement may be helpful for level selection in ischemic amputations.

Publication Types:
- Clinical Trial

PMID: 10641999 [PubMed - indexed for MEDLINE]

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1: Essays Biochem. 2002;38:95-111.

Proteases in blood clotting.

Walsh PN, Ahmad SS.

Sol Sherry Thrombosis Research Center, Temple University School of Medicine, 3400 North Broad Street, Philadelphia, PA 19140, USA. pnw@astro.temple.edu

The serine proteases, cofactors and cell-receptor molecules that comprise the haemostatic mechanism are highly conserved modular proteins that have evolved to participate in biochemical reactions in blood coagulation, anticoagulation and fibrinolysis. Blood coagulation is initiated by exposure of tissue factor, which forms a complex with factor VIIa and factor X, which results in the generation of small quantities of thrombin and is rapidly shutdown by the tissue factor pathway inhibitor. The generation of these small quantities of thrombin then activates factor XI, resulting in a sequence of events that lead to the activation of factor IX, factor X and prothrombin. Sufficient thrombin is generated to effect normal haemostasis by converting fibrinogen into fibrin. The anticoagulant pathways that regulate blood coagulation include the protein C anticoagulant mechanism, the serine protease inhibitors in plasma, and the Kunitz-like inhibitors, tissue factor pathway inhibitor and protease nexin 2. Finally, the fibrinolytic mechanism that comprises the activation of plasminogen into plasmin prevents excessive fibrin accumulation by promoting local dissolution of thrombi and promoting wound healing by reestablishment of blood flow.

Publication Types:
- Review
- Review, Tutorial

PMID: 12463164 [PubMed - indexed for MEDLINE]

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L3   ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2004 ACS on STN
2003:455010  Document No. 139:989  Methods of use of recombinant vasoactive
     protein from salivary gland of the black fly.  Cupp,
     Mary Smith; Cupp, Eddie Wayne; Swaim, Steven F. (Auburn University, USA).
     U.S. Pat. Appl. Publ. US 2003109447 A1 20030612, 23 pp., Cont.-in-part of
     U.S. Ser. No. 218,699.  (English).  CODEN: USXXCO.  APPLICATION: US
     2002-288740 20021106.  PRIORITY: US 1997-PV40418 19970313; US 1998-36355
     19980306; US 2000-702647 20001031; US 2002-218699 20020814.
AB   The invention is drawn to vasodilative proteins from the salivary glands
     of the species Simulium vittatum.  The protein addnl. has immunomodulating
     activities.  Methods for recombinant production of the protein as well as
     biomedical uses are provided.

L3   ANSWER 2 OF 8  SCISEARCH  COPYRIGHT (c) 2004 The Thomson Corporation.  on
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2003:1083807  The Genuine Article (R) Number: 750CL. Vasodilatory activity in
     horsefly and deerfly salivary glands.  Rajska P; Pechanova O; Takac P;
     Kazimirova M; Roller L; Vidlicka L; Ciampor F; Labuda M; Nuttall P A
     (Reprint). NERC, CEH Inst Virol & Environm Microbiol, Mansfield Rd, Oxford
     OX1 3SR, England (Reprint); NERC, CEH Inst Virol & Environm Microbiol,
     Oxford OX1 3SR, England; Slovak Acad Sci, Inst Normal & Pathol Physiol,
     Bratislava, Slovakia; Slovak Acad Sci, Inst Zool, Bratislava, Slovakia.
     MEDICAL AND VETERINARY ENTOMOLOGY (DEC 2003) Vol. 17, No. 4, pp. 395-402.
     Publisher: BLACKWELL PUBLISHING LTD. 9600 GARSINGTON RD, OXFORD OX4 2DG,
     OXON, ENGLAND. ISSN: 0269-283X. Pub. country: England; Slovakia. Language:
     English.
     *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
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AB Salivary gland extract (SGE) of four horsefly species (Hybomitra bimaculata Macquart, Hybomitra ciureai Seguy, Tabanus bromius L., Tabanus glaucopis Meigen) and one deerfly species (Chrysops relictus Meigen) (Diptera: Tabanidae) were shown to contain vasodilatory activity. Aliquots equivalent to 1, 5 and 10 pairs of salivary glands (SG) relaxed rat femoral artery (with intact endothelium) pre-constricted with phenylephrine. Vasodilatory activity was dose-dependent. SGE of one horsefly species (Haematopota pluvialis L.) did not induce relaxation. The kinetics of vasodilation induced by SGE of four horsefly species differed from the deerfly. These results indicate that tabanid species may produce more than one type of **vasodilator** to aid blood feeding.

L3 ANSWER 3 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
2003:85888 Document No.: PREV200300085888. Recombinant vasoactive protein from salivary gland of the **black fly.** Cupp, Mary S. [Inventor, Reprint Author]; Ribeiro, Jose M. C. [Inventor]; Cupp, Eddie W. [Inventor]. ASSIGNEE: Auburn University; The University of Arizona, Tucson, AZ, USA. Patent Info.: US 6500420 December 31, 2002. Official Gazette of the United States Patent and Trademark Office Patents, (Dec 31 2002) Vol. 1265, No. 5. http://www.uspto.gov/web/menu/patdata.html. e-file.
ISSN: 0098-1133 (ISSN print). Language: English.
AB The invention is drawn to vasodilative proteins from the salivary glands of the species, Simulium. The protein additionally has immunomodulating activities. Methods for recombinant production of the protein as well as biomedical uses are provided.

L3 ANSWER 4 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
2001:493503 Document No.: PREV200100493503. Serum IgG from pemphigus foliaceus patients reacts against maxadilan. Roselino, A. [Reprint author]; Figueiredo, J. [Reprint author]; Kounga, K.; Reddy, V.; Lerner, E.. Internal Medicine, Faculty of Medicine, University of Sao Paulo, Ribeirao Preto, SP, Brazil. Journal of Investigative Dermatology, (August, 2001) Vol. 117, No. 2, pp. 460. print.
Meeting Info.: 62nd Annual Meeting of the Society for Investigative Dermatology. Washington, DC, USA. May 09-12, 2001.
CODEN: JIDEAE. ISSN: 0022-202X. Language: English.

L3 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
1998:629985 Document No. 129:259343 Recombinant vasoactive protein from salivary gland of the **black fly.** Cupp, Mary S.; Ribeiro, Jose M. C.; Cupp, Eddie W.; Swaim, Steven F. (Auburn University, USA). PCT Int. Appl. WO 9840089 A1 19980917, 28 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US4795 19980312. PRIORITY: US 1997-40418 19970313; US 1998-36355 19980306.
AB The invention is drawn to vasodilative proteins from the salivary glands of the species, Simulium. The protein addnl. has immunomodulating activities. Methods for recombinant production of the protein as well as biomedical uses are provided.

L3 ANSWER 6 OF 8 MEDLINE on STN
1998225234. PubMed ID: 9556538. Analyses of cDNA and recombinant protein for a potent vasoactive protein in saliva of a blood-feeding **black fly**, Simulium vittatum. Cupp M S; Ribeiro J M; Champagne D E; Cupp E W. (Department of Entomology, University of Arizona, Tucson, AZ 85721, USA.. mcupp@acesag.auburn.edu) . Journal of experimental biology, (1998 May) 201 (Pt 10) 1553-61. Journal code: 0243705. ISSN: 0022-0949. Pub. country: ENGLAND: United Kingdom. Language: English.
AB A cDNA was cloned from the salivary glands of a blood-feeding

black fly Simulium vittatum. The encoded protein has been given the name Simulium vittatum erythema protein or SVEP, because of its ability to increase blood perfusion in skin capillaries, resulting in the well-characterized erythema of **black fly** bites. The full-length cDNA contains 548 base pairs which encode 152 amino acid residues of the nascent protein. Post-translational processing produces a mature, secreted protein of 133 residues with a molecular mass of 15.4 kDa. Recombinant SVEP (rSVEP) was produced in a baculovirus expression system and purified by a one-step reversed-phase HPLC procedure. Analyses of physical properties and biological potency demonstrated fidelity of rSVEP to the native protein. Recombinant SVEP relaxed rabbit aorta preparations when preconstricted with 2 micromol l-1 phenylephrine or 25 mmol l-1 K+ but not with 60 mmol l-1 K+. Further, the rSVEP-induced relaxation response of phenylephrine-constricted aorta was inhibited by glibenclamide (10 micromol l-1), suggesting that at least part of its action to relax smooth muscle may result from the opening of ATP-dependent K+ channels. SVEP is a novel salivary-gland-derived vasoactive protein that may be essential for blood feeding by **black flies** and could potentially enhance transmission of filarial parasites.

L3 ANSWER 7 OF 8 MEDLINE on STN DUPLICATE 1
97257080. PubMed ID: 9103750. **Black fly** (Diptera:Simuliidae) salivary secretions: importance in vector competence and disease. Cupp E W; Cupp M S. (Department of Entomology, Auburn University, AL 36849-5413, USA.) Journal of medical entomology, (1997 Mar) 34 (2) 87-94. Ref: 76. Journal code: 0375400. ISSN: 0022-2585. Pub. country: United States. Language: English.

AB When blood-feeding, **black flies** introduce secretions into the feeding lesion that act in a coordinated manner on the 3 arms of the vertebrate hemostatic system (platelet aggregation, coagulation, and vasoconstriction). Apyrase activity inhibits platelet aggregation and is ubiquitous in the saliva of **black flies**, although activity per gland varies by species and has a positive association with anthropophagy. Anticoagulants target components in the final common pathway of the coagulation cascade, including factors V, Xa, and II (thrombin). The antithrombin salivary protein may exert a redundant effect by inhibiting the role of thrombin in platelet aggregation. Antithrombin presence and activity also varies among **black fly** species, and exhibits a positive correlation with zoophagy. Vasodilation of capillaries to increase blood supply to the feeding wound appears to be an important requirement for Simulium spp., because substantial erythema-inducing activity, has been demonstrated in salivary glands of all New World species examined. Salivary glands of Simulium ochraceum (Walker), a highly anthropophilic vector of Onchocerca volvulus (Leuckhart), contain greater **vasodilator** activity than several other species, including S. metallicum Bellardi, a secondary zoophagic vector of human onchocerciasis. Simulium vittatum Zetterstedt saliva affects immune cell responses and cytokine production. The ability of the saliva to modulate components of the host immune system provides an opportunity for enhancing transmission of pathogens during bloodfeeding. Thus, the likely possibility that effective pathogen transmission relies on vector saliva may complement present efforts aimed at target epitopes of O. volvulus or identify additional molecules to be investigated as part of a "river blindness" vaccine cocktail. Components in saliva also may enhance the transmission of other microbial agents either by a cofeeding process similar to that observed in ixodid ticks or through rupture of the labrum during escape of Onchocerca infective stage larvae. In a few instances, saliva of some Simulium spp. also has been associated with extensive tissue and organ pathology, including hemorrhagic shock and death. Pathologic signs associated with this syndrome indicate an enhanced antihemostatic activity in saliva.

L3 ANSWER 8 OF 8 MEDLINE on STN DUPLICATE 2
94161217. PubMed ID: 8116819. Vasodilative activity in **black fly** salivary glands. Cupp M S; Ribeiro J M; Cupp E W. (Department

of Veterinary Science, University of Arizona, Tucson.) American journal of tropical medicine and hygiene, (1994 Feb) 50 (2) 241-6. Journal code: 0370507. ISSN: 0002-9637. Pub. country: United States. Language: English.

AB Salivary gland extracts of several Simulium spp. were shown to contain vasodilative activity as measured by the rapid and persistent induction of erythema in response to intradermal injection into rabbit skin. Total salivary gland activities were approximately equal for S. vittatum, S. metallicum, S. bivittatum, and S. argus (titers of 0.03-0.02 pairs of gland). Total gland activity in the highly anthropophilic species S. ochraceum, however, was an order of magnitude greater, with erythema produced by as little as 0.002 pairs of glands. Tests for physical stability of the activities from two species (S. vittatum and S. ochraceum) indicated that the **vasodilators** were proteinaceous and heat stable. A two-step, reversed-phase high-performance liquid chromatography (HPLC) procedure was developed that isolated both activities with similar elution patterns. Homogeneity of the purified protein from S. vittatum was confirmed by capillary gel electrophoresis. Electrospray ionization mass spectroscopy of the S. vittatum protein detected a mass of 15,351 daltons. Similarity in elution times of the proteins from a TSK HPLC column predict some structural similarities between the S. vittatum and S. ochraceum **vasodilator** proteins.

=> s l1 and wound healing
L4 255 L1 AND WOUND HEALING

=> s l4 and surgical wound
L5 4 L4 AND SURGICAL WOUND

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L6 4 DUP REMOVE L5 (0 DUPLICATES REMOVED)

=> d l6 1-4 cbib abs

L6 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
2003:633053 Document No. 139:169383 Novel **wound healing** composition not containing bovine-derived activating reagents. Britton, Calvin; Dellinger, Alex; Limbird, Jim; Keller, Carl; Worden, Charles (USA). U.S. Pat. Appl. Publ. US 2003152639 A1 20030814, 7 pp., Cont.-in-part of U.S. Ser. No. 898,316, abandoned. (English). CODEN: USXXCO. APPLICATION: US 2002-323861 20021217. PRIORITY: US 2001-898316 20010703.

AB A wound care preparation free from bovine-derived activating agents is disclosed for use in wound care, for both topical wounds and **surgical wounds.** The preparation is isolated by first obtaining an amount of whole blood from the patient and treating the whole blood with one or more anti-clotting agents, subjecting the whole blood to a centrifugation process to obtain an amount of platelet-rich plasma, adding to the platelet-rich plasma an amount of anti-clotting neutralizing agent, and mixing the platelet-rich plasma with a structural matrix to increase viscosity of the preparation In use, the viscous preparation can be applied directly to a wound or surgery incision and the viscous preparation may be mixed with other **wound healing** agents, growth matrixes, or promoters such as antifungal agents, antibiotics, and preservatives. For example, platelet-rich plasma (PRP) was obtained and combined with one part powdered vitamin C and 3 parts chitosan. After several minutes a golden colored gel was formed. The gel can be applied to the wound bed and remainder stored and refrigerated for at least 5-7 days (the viable life span of a platelet) and subsequently used. Gel viscosity can be controlled by (i) adding more PRP to make the gel less viscous, (ii) adding less vitamin C to decrease the acidity therefore decrease viscosity, or (iii) adding more vitamin C to increase acidity and therefore increase viscosity.

L6 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
2003:23353 Document No. 138:49970 Novel **wound healing** composition not containing bovine-derived activating reagents. Britton, Calvin; Dellinger, Alex; Limbird, Jim; Keller, Carl; Worden, Charles (USA). U.S. Pat. Appl. Publ. US 2003007957 A1 20030109, 7 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-898316 20010703.

AB A wound care preparation free from bovine-derived activating agents is disclosed for use in wound care, for both topical wounds and **surgical wounds.** The preparation is isolated by first obtaining an amount of whole blood from the patient and treating the whole blood with one or more anti-clotting agents, subjecting the whole blood to a centrifugation process to obtain an amount of platelet-rich plasma, adding to the platelet-rich plasma an amount of anti-clotting neutralizing agent, and mixing the platelet-rich plasma with a structural matrix to increase viscosity of the preparation In use, the viscous preparation can be applied directly to a wound or surgery incision and the viscous preparation may be mixed with other **wound healing** agents, growth matrixes, or promoters such as anti-fungal agents, anti-biotic agents, and preservatives.

L6 ANSWER 3 OF 4 MEDLINE on STN
2003146402. PubMed ID: 12661250. [Application of viable cryopreserved alloderm transplants in the treatment of wound defects of soft tissues]. Ispol'zovanie zhiznesposobnykh kriokonservirovannykh allodermotransplantatov v lechenii ranevykh defektov miagkikh tkanei. Khrupkin V I; Ivashkin A N; Pisarenko L V; Nizovoi A V; Fominykh E M; Kiselev I V; Kuzin A N; Fedorov D N; Vasil'ev A V; Terskikh V V. Vestnik khirurgii imeni I. I. Grekova, (2002) 161 (5) 55-9. Journal code: 0411377. ISSN: 0042-4625. Pub. country: Russia: Russian Federation. Language: Russian.

AB An original method is proposed for treatment of long-standing intractable wounds and trophic ulcers using viable cryopreserved allodermotransplants and a distant air-plasma treatment. The main source of the allodermotransplants is the cadaverous skin. It was shown that the cadaverous skin taken during 17 hours after the donor's death was viable. The maximum period for storage of the viable skin when the worked out preservative is used at the temperature regimen -18 degrees C is 10 days, and at -70 degrees C it can be as long as 45 days. The analysis performed included 101 patients with long-standing intractable wounds and trophic ulcers. In 51 of them the new worked out method was used. An analysis of clinical and histomorphological data has proved that the application of the viable cryopreserved allodermotransplants and distant air-plasma treatment favor the better course of reparative processes. By the end of the forth week the wounds were completely closed in 19.7% of patients, the wound areas were considerably less (more than by 50% of the initial size) in 43.1%, less reduction of the wound area (less than 50% of the initial size) in 27.4%, in 9.8% there was no effect. No negative results were noted. It should be noted that closure of the tissue defect can be achieved by stimulation of the physiological regeneration of the patient's tissues. This method of regeneration of the skin is effective in trophic ulcers, long-standing intractable wounds and is also recommended in case of deficit of donor resources or when the severe state of the patient does not allow active surgical treatment.

L6 ANSWER 4 OF 4 MEDLINE on STN
1999369787. PubMed ID: 10441101. Preferential impairment of nitric oxide-mediated endothelium-dependent relaxation in human cervical arteries after irradiation. Sugihara T; Hattori Y; Yamamoto Y; Qi F; Ichikawa R; Sato A; Liu M Y; Abe K; Kanno M. (Department of Plastic and Reconstructive Surgery, Hokkaido University School of Medicine, Sapporo, Japan.) Circulation, (1999 Aug 10) 100 (6) 635-41. Journal code: 0147763. ISSN: 1524-4539. Pub. country: United States. Language: English.

AB BACKGROUND: Vascular abnormalities are a major cause of postoperative complications in irradiated tissues. Endothelial cell dysfunction characterized by diminished endothelium-dependent relaxation may be

involved. We examined the endothelium-dependent relaxation and morphology of the endothelium in irradiated human cervical arteries. METHODS AND RESULTS: Irradiated arteries were taken from the neck region of patients who had radiation therapy. Arteries from patients who did not receive radiation therapy were used as controls. Endothelium-dependent relaxation to acetylcholine and A23187 was impaired in irradiated arteries. Norepinephrine-induced contraction and sodium nitroprusside-induced relaxation were unchanged. In control arteries, N(omega)-nitro-L-arginine and indomethacin each caused a partial inhibition of endothelium-dependent relaxation. In irradiated arteries, the impaired endothelium-dependent relaxation was unaffected by these agents, but it was abolished by high K(+). Acetylcholine produced similar degrees of hyperpolarization in control and irradiated arteries. Immunohistochemical examination for endothelial nitric oxide synthase indicated no expression in the endothelium of irradiated arteries. Electron scanning microscopy showed morphologically intact endothelial cells in irradiated arteries. CONCLUSIONS: In irradiated human cervical arteries, the nitric oxide- and prostacyclin-mediated endothelium-dependent relaxation, but not endothelium-derived hyperpolarizing factor-mediated relaxation, are specifically impaired, without significant morphological damage of the endothelium. The impaired nitric oxide-mediated relaxation was associated with a lack of endothelial nitric oxide synthase expression. Our results suggest the importance of impaired endothelial function in irradiated human blood vessels, which may partly explain the development of vascular stenosis and poor **surgical wound healing** in irradiated tissues.

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=> s l4 and heart failure
L7            2 L4 AND HEART FAILURE

=> dup remove l7
PROCESSING COMPLETED FOR L7
L8            2 DUP REMOVE L7 (0 DUPLICATES REMOVED)

=> d l8 1-2 cbib abs
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L8 ANSWER 1 OF 2 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

2004076270 EMBASE Postoperative management in patients with complex congenital heart disease. Tweddell J.S.; Hoffman G.M.. Dr. J.S. Tweddell, Division of Cardiothoracic Surgery, Children's Hospital of Wisconsin, 9000 W. Wisconsin Ave., Milwaukee, WI 53226, United States. Pediatric Cardiac Surgery Annual 5/- (187-205) 2002.

Refs: 127.

ISSN: 1092-9126. CODEN: STCSFS. Pub. Country: United States. Language: English. Summary Language: English.

AB Life-threatening problems occur in the neonate and infant after cardiac surgery because of the interplay of diminished cardiac output (CO), increased metabolic demand, inflammatory responses to cardiopulmonary bypass, and maladaptive responses to stress. Therefore, the postoperative management of patients with complex congenital heart defects is directed at optimization of oxygen delivery to maintain end-organ function and promote **wound healing.** Traditionally, assessment of circulation in the postoperative congenital heart patient has depended on indirect assessment of CO using parameters such as blood pressure, pulses, capillary refill, and urine output. Because of the limitations of indirect and observer-dependent assessment of CO, we rely on objective measures of tissue oxygen levels for the complex postoperative patient. We have found that continuous monitoring of the mixed venous saturation (SvO(2)) allows for identification of acute changes in systemic oxygen delivery and frequently precedes other indicators of decreased CO. The postoperative patient can be expected to have a period of decreasing CO, and the need for intervention should be anticipated because critical low output syndrome will develop in a subset of patients. Strategies for

postoperative care are developed based on the diagnosis and procedure, but optimizing SvO(2) is a consistent goal. A uniform approach to airway maintenance, vascular access, and drug infusions, all universal concerns during the perioperative period, minimizes the potential for these predictable and necessary interventions to result in morbidity or mortality. Management of the postoperative single ventricle patient targets stabilization of the systemic vascular resistance through the use of **vasodilators** to improve systemic perfusion and simplify ventilator management. Management of any individual patient should be driven by objective analysis of available data and must include efforts to re-evaluate the treatment plan as well as to identify unanticipated problems. Copyright .COPYRGT. 2002 by W.B. Saunders Company.

L8 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
1999:489873 Document No. 131:345958 WRC-0470 (Discovery Therapeutics). Zaza, Antonio (Department of Physiology and Biochemistry, University of Milan, Milan, 20133, Italy). Current Opinion in Cardiovascular, Pulmonary & Renal Investigational Drugs, 1(2), 301-306 (English) 1999. CODEN: CCPRFX. ISSN: 1464-8482. Publisher: Current Drugs Ltd..
AB A review with 24 refs. Discovery Therapeutics has synthesized, and is evaluating the potential of, a series of adenosine A2A agonists for the treatment of coronary artery disease, congestive **heart failure**, wounds, and restenosis. The lead compound of the collaboration with Medco, MRE-0470 (WRC-0470), was approved for phase I trials in Jan. 1999, for use as a selective coronary **vasodilator** during myocardial perfusion imaging procedures to diagnose coronary artery disease. It will thus be developed as a pharmacol. stressor in the diagnosis and treatment of coronary artery disease, and will be commercialized as a follow-on to Medco Research's Adenoscan, while other agonists in the library will be investigated and evaluated for effects on coronary artery disease, congestive **heart failure**, **wound healing**, and restenosis following angioplasty.

=> s l1 and surgical wound
L9 7 L1 AND SURGICAL WOUND

=> dup remove l9
PROCESSING COMPLETED FOR L9
L10 6 DUP REMOVE L9 (1 DUPLICATE REMOVED)

=> d l10 1-6 cbib abs

L10 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2003:633053 Document No. 139:169383 Novel wound healing composition not containing bovine-derived activating reagents. Britton, Calvin; Dellinger, Alex; Limbird, Jim; Keller, Carl; Worden, Charles (USA). U.S. Pat. Appl. Publ. US 2003152639 A1 20030814, 7 pp., Cont.-in-part of U.S. Ser. No. 898,316, abandoned. (English). CODEN: USXXCO. APPLICATION: US 2002-323861 20021217. PRIORITY: US 2001-898316 20010703.
AB A wound care preparation free from bovine-derived activating agents is disclosed for use in wound care, for both topical wounds and **surgical wounds.** The preparation is isolated by first obtaining an amount of whole blood from the patient and treating the whole blood with one or more anti-clotting agents, subjecting the whole blood to a centrifugation process to obtain an amount of platelet-rich plasma, adding to the platelet-rich plasma an amount of anti-clotting neutralizing agent, and mixing the platelet-rich plasma with a structural matrix to increase viscosity of the preparation In use, the viscous preparation can be applied directly to a wound or surgery incision and the viscous preparation may be mixed with other wound healing agents, growth matrixes, or promoters such as antifungal agents, antibiotics, and preservatives. For example, platelet-rich plasma (PRP) was obtained and combined with one part powdered vitamin C and 3 parts chitosan. After several minutes a golden colored gel was formed. The gel can be applied to the wound bed and remainder

stored and refrigerated for at least 5-7 days (the viable life span of a platelet) and subsequently used. Gel viscosity can be controlled by (i) adding more PRP to make the gel less viscous, (ii) adding less vitamin C to decrease the acidity therefore decrease viscosity, or (iii) adding more vitamin C to increase acidity and therefore increase viscosity.

L10 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2003:23353 Document No. 138:49970 Novel wound healing composition not containing bovine-derived activating reagents. Britton, Calvin; Dellinger, Alex; Limbird, Jim; Keller, Carl; Worden, Charles (USA). U.S. Pat. Appl. Publ. US 2003007957 A1 20030109, 7 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-898316 20010703.

AB A wound care preparation free from bovine-derived activating agents is disclosed for use in wound care, for both topical wounds and **surgical wounds.** The preparation is isolated by first obtaining an amount of whole blood from the patient and treating the whole blood with one or more anti-clotting agents, subjecting the whole blood to a centrifugation process to obtain an amount of platelet-rich plasma, adding to the platelet-rich plasma an amount of anti-clotting neutralizing agent, and mixing the platelet-rich plasma with a structural matrix to increase viscosity of the preparation In use, the viscous preparation can be applied directly to a wound or surgery incision and the viscous preparation may be mixed with other wound healing agents, growth matrixes, or promoters such as anti-fungal agents, anti-biotic agents, and preservatives.

L10 ANSWER 3 OF 6 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
2004:194041 Document No.: PREV200400194601. Effects of blood pressure lowering doses of gamma - aminobutyric acid (GABA) on local cerebral blood flow in the rat. Liu, X. [Reprint Author]; Esaki, T. [Reprint Author]; Cook, M. [Reprint Author]; Jehle, J. [Reprint Author]; Sokoloff, L. [Reprint Author]. Lab. of Cerebral Metabolism, Natl. Inst. of Mental Hlth., Natl. Inst. of Hlth., Bethesda, MD, USA. Society for Neuroscience Abstract Viewer and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. 107.1. http://sfn.scholarone.com. e-file.
Meeting Info.: 33rd Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 08-12, 2003. Society of Neuroscience.
Language: English.

AB GABA, a major inhibitory transmitter in the CNS, is widely distributed in the brain. It has long been known that intravenously or orally administered GABA significantly lowers blood pressure in animals and humans. The present studies were carried out to determine if this depression in blood pressure is sufficient to affect local cerebral blood flow (CBF) and thus also cerebral functions. Local cerebral blood flow was determined quantitatively in normal, conscious, adult, male Sprague-Dawley rats by the autoradiographic (14C)iodoantipyrine method. Under halothane anesthesia polyethylene catheters were inserted into both femoral arteries and veins, and after closure of the **surgical wound**, the anesthesia was discontinued, and at least three hours were allowed for recovery. GABA was infused intravenously for 20 minutes and continued through the subsequent one minute during which CBF was determined. Mean arterial blood pressure (MABP) was monitored continuously throughout the procedure. GABA administered intravenously at doses of 1.5, 3.0, and 6.0 mg/kg/min lowered MABP by 2%, 11% and 19%, respectively. Local CBF, however, was not changed significantly ($p>0.05$) in any of the 21 brain structures examined. Apparently, cerebral vasodilatation due to autoregulatory mechanisms and/or direct **vasodilator** effects of GABA on cerebral blood vessels, like those in the systemic vessels causing the fall in MABP, was sufficient to maintain CBF despite the decline in MABP. The nature of the mechanisms underlying the effects of GABA on MABP is being investigated.Key Words: (14C)iodoantipyrine/autoregulation/quantitative autoradiography /brain.

L10 ANSWER 4 OF 6 MEDLINE on STN
2003146402. PubMed ID: 12661250. [Application of viable cryopreserved alloderm transplants in the treatment of wound defects of soft tissues].

Ispol'zovanie zhiznesposobnykh kriokonservirovannykh allodermotransplantatov v lechenii ranevykh defektov miagkikh tkanei. Khrupkin V I; Ivashkin A N; Pisarenko L V; Nizovoi A V; Fominykh E M; Kiselev I V; Kuzin A N; Fedorov D N; Vasil'ev A V; Terskikh V V. Vestnik khirurgii imeni I. I. Grekova, (2002) 161 (5) 55-9. Journal code: 0411377. ISSN: 0042-4625. Pub. country: Russia: Russian Federation. Language: Russian.

AB An original method is proposed for treatment of long-standing intractable wounds and trophic ulcers using viable cryopreserved allodermotransplants and a distant air-plasma treatment. The main source of the allodermotransplants is the cadaverous skin. It was shown that the cadaverous skin taken during 17 hours after the donor's death was viable. The maximum period for storage of the viable skin when the worked out preservative is used at the temperature regimen -18 degrees C is 10 days, and at -70 degrees C it can be as long as 45 days. The analysis performed included 101 patients with long-standing intractable wounds and trophic ulcers. In 51 of them the new worked out method was used. An analysis of clinical and histomorphological data has proved that the application of the viable cryopreserved allodermotransplants and distant air-plasma treatment favor the better course of reparative processes. By the end of the forth week the wounds were completely closed in 19.7% of patients, the wound areas were considerably less (more than by 50% of the initial size) in 43.1%, less reduction of the wound area (less than 50% of the initial size) in 27.4%, in 9.8% there was no effect. No negative results were noted. It should be noted that closure of the tissue defect can be achieved by stimulation of the physiological regeneration of the patient's tissues. This method of regeneration of the skin is effective in trophic ulcers, long-standing intractable wounds and is also recommended in case of deficit of donor resources or when the severe state of the patient does not allow active surgical treatment.

L10 ANSWER 5 OF 6 MEDLINE on STN

1999369787. PubMed ID: 10441101. Preferential impairment of nitric oxide-mediated endothelium-dependent relaxation in human cervical arteries after irradiation. Sugihara T; Hattori Y; Yamamoto Y; Qi F; Ichikawa R; Sato A; Liu M Y; Abe K; Kanno M. (Department of Plastic and Reconstructive Surgery, Hokkaido University School of Medicine, Sapporo, Japan.) Circulation, (1999 Aug 10) 100 (6) 635-41. Journal code: 0147763. ISSN: 1524-4539. Pub. country: United States. Language: English.

AB BACKGROUND: Vascular abnormalities are a major cause of postoperative complications in irradiated tissues. Endothelial cell dysfunction characterized by diminished endothelium-dependent relaxation may be involved. We examined the endothelium-dependent relaxation and morphology of the endothelium in irradiated human cervical arteries. METHODS AND RESULTS: Irradiated arteries were taken from the neck region of patients who had radiation therapy. Arteries from patients who did not receive radiation therapy were used as controls. Endothelium-dependent relaxation to acetylcholine and A23187 was impaired in irradiated arteries. Norepinephrine-induced contraction and sodium nitroprusside-induced relaxation were unchanged. In control arteries, N(omega)-nitro-L-arginine and indomethacin each caused a partial inhibition of endothelium-dependent relaxation. In irradiated arteries, the impaired endothelium-dependent relaxation was unaffected by these agents, but it was abolished by high K(+). Acetylcholine produced similar degrees of hyperpolarization in control and irradiated arteries. Immunohistochemical examination for endothelial nitric oxide synthase indicated no expression in the endothelium of irradiated arteries. Electron scanning microscopy showed morphologically intact endothelial cells in irradiated arteries. CONCLUSIONS: In irradiated human cervical arteries, the nitric oxide- and prostacyclin-mediated endothelium-dependent relaxation, but not endothelium-derived hyperpolarizing factor-mediated relaxation, are specifically impaired, without significant morphological damage of the endothelium. The impaired nitric oxide-mediated relaxation was associated with a lack of endothelial nitric oxide synthase expression. Our results suggest the importance of impaired endothelial function in irradiated

human blood vessels, which may partly explain the development of vascular stenosis and poor **surgical wound** healing in irradiated tissues.

L10 ANSWER 6 OF 6 MEDLINE on STN DUPLICATE 1
1999137057. PubMed ID: 9972772. The effects of prostaglandin E1 on intraoperative temperature changes and the incidence of postoperative shivering during deliberate mild hypothermia for neurosurgical procedures.
Kawaguchi M; Inoue S; Sakamoto T; Kawaraguchi Y; Furuya H; Sakaki T.
(Department of Anesthesiology, Nara Medical University, Japan.)
Anesthesia and analgesia, (1999 Feb) 88 (2) 446-51. Journal code: 1310650. ISSN: 0003-2999. Pub. country: United States. Language: English.
AB We investigated the effects of i.v. prostaglandin E1 (PGE1) on intraoperative changes of core temperature and the incidence of postoperative shivering in neurosurgical patients undergoing deliberate mild hypothermia. Eighty-three patients were randomly assigned to one of three groups: patients in the control group did not receive PGE1, whereas patients in the PG20 group and PG50 group received PGE1 at a dose of 0.02 and 0.05 microg x kg(-1) x min(-1), respectively. The administration of PGE1 was started just after the induction of anesthesia and continued until the end of anesthesia. Anesthesia was maintained with nitrous oxide in oxygen, sevoflurane, and fentanyl. After the induction of anesthesia, patients were cooled using a water blanket and a convective device blanket. Tympanic membrane temperature was maintained at 34.5 degrees C. During **surgical wound** closure, patients were rewarmed. Intraoperative changes in tympanic membrane and skin temperatures and the incidence of postoperative shivering were compared among groups. Demographic and intraoperative variables were similar among groups. There were no significant differences in tympanic temperatures among groups at each point during the operation. Skin temperature 30 min after rewarming and just after tracheal extubation was significantly lower in the PG20 group than in the PG50 group. Postoperative shivering was more frequent in the PG20 group (43%) than in the control (13%) and PG50 (17%) groups. These results suggest that the intraoperative administration of PGE1 does not affect changes in core temperature during deliberate mild hypothermia and that PGE1 at a dose of 0.02 microg x kg(-1) x min(-1) may increase the occurrence of postoperative shivering. Implications: Deliberate mild hypothermia has been proposed as a means of providing cerebral protection during neurosurgical procedures. Vasodilating drugs may be used during deliberate mild hypothermia to maintain peripheral circulation and to enhance the cooling and rewarming rate. In the present study, however, we found no benefit from i.v. prostaglandin E1 administration during deliberate mild hypothermia in neurosurgical patients.

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=> s l1 and heart failure
L11      12435 L1 AND HEART FAILURE

=> s l11 and promotes wound healing
L12          0 L11 AND PROMOTES WOUND HEALING

=> du remove l11
DU IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s (cupp m?/au or ribeiro j?/au or cupp e?/au or swaim s?/au)
L13       4030 (CUPP M?/AU OR RIBEIRO J?/AU OR CUPP E?/AU OR SWAIM S?/AU)

=> s l13 and black fly
L14        122 L13 AND BLACK FLY

=> s l14 and vasodilator
L15         11 L14 AND VASODILATOR
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=> dup remove l15
PROCESSING COMPLETED FOR L15
L16 6 DUP REMOVE L15 (5 DUPLICATES REMOVED)

=> d l16 1-6 cbib abs

L16 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2003:455010 Document No. 139:989 Methods of use of recombinant vasoactive protein from salivary gland of the **black fly.**
Cupp, Mary Smith; Cupp, Eddie Wayne; Swaim, Steven F. (Auburn University, USA). U.S. Pat. Appl. Publ. US 2003109447 A1 20030612, 23 pp., Cont.-in-part of U.S. Ser. No. 218,699. (English). CODEN: USXXCO. APPLICATION: US 2002-288740 20021106. PRIORITY: US 1997-PV40418 19970313; US 1998-36355 19980306; US 2000-702647 20001031; US 2002-218699 20020814.
AB The invention is drawn to vasodilative proteins from the salivary glands of the species Simulium vittatum. The protein addnl. has immunomodulating activities. Methods for recombinant production of the protein as well as biomedical uses are provided.

L16 ANSWER 2 OF 6 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
2003:85888 Document No.: PREV200300085888. Recombinant vasoactive protein from salivary gland of the **black fly. Cupp, Mary S.** [Inventor, Reprint Author]; **Ribeiro, Jose M. C.** [Inventor]; **Cupp, Eddie W.** [Inventor]. ASSIGNEE: Auburn University; The University of Arizona, Tucson, AZ, USA. Patent Info.: US 6500420 December 31, 2002. Official Gazette of the United States Patent and Trademark Office Patents, (Dec 31 2002) Vol. 1265, No. 5. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print). Language: English.
AB The invention is drawn to vasodilative proteins from the salivary glands of the species, Simulium. The protein additionally has immunomodulating activities. Methods for recombinant production of the protein as well as biomedical uses are provided.

L16 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
1998:629985 Document No. 129:259343 Recombinant vasoactive protein from salivary gland of the **black fly. Cupp, Mary S.; Ribeiro, Jose M. C.; Cupp, Eddie W.; Swaim, Steven F.** (Auburn University, USA). PCT Int. Appl. WO 9840089 A1 19980917, 28 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US4795 19980312. PRIORITY: US 1997-40418 19970313; US 1998-36355 19980306.
AB The invention is drawn to vasodilative proteins from the salivary glands of the species, Simulium. The protein addnl. has immunomodulating activities. Methods for recombinant production of the protein as well as biomedical uses are provided.

L16 ANSWER 4 OF 6 MEDLINE on STN
1998225234. PubMed ID: 9556538. Analyses of cDNA and recombinant protein for a potent vasoactive protein in saliva of a blood-feeding **black fly**, Simulium vittatum. **Cupp M S; Ribeiro J M;** Champagne D E; **Cupp E W.** (Department of Entomology, University of Arizona, Tucson, AZ 85721, USA.. mcupp@acesag.auburn.edu) . Journal of experimental biology, (1998 May) 201 (Pt 10) 1553-61. Journal code: 0243705. ISSN: 0022-0949. Pub. country: ENGLAND: United Kingdom. Language: English.
AB A cDNA was cloned from the salivary glands of a blood-feeding

black fly Simulium vittatum. The encoded protein has been given the name Simulium vittatum erythema protein or SVEP, because of its ability to increase blood perfusion in skin capillaries, resulting in the well-characterized erythema of **black fly** bites. The full-length cDNA contains 548 base pairs which encode 152 amino acid residues of the nascent protein. Post-translational processing produces a mature, secreted protein of 133 residues with a molecular mass of 15.4 kDa. Recombinant SVEP (rSVEP) was produced in a baculovirus expression system and purified by a one-step reversed-phase HPLC procedure. Analyses of physical properties and biological potency demonstrated fidelity of rSVEP to the native protein. Recombinant SVEP relaxed rabbit aorta preparations when preconstricted with 2 micromol l-1 phenylephrine or 25 mmol l-1 K+ but not with 60 mmol l-1 K+. Further, the rSVEP-induced relaxation response of phenylephrine-constricted aorta was inhibited by glibenclamide (10 micromol l-1), suggesting that at least part of its action to relax smooth muscle may result from the opening of ATP-dependent K+ channels. SVEP is a novel salivary-gland-derived vasoactive protein that may be essential for blood feeding by **black flies** and could potentially enhance transmission of filarial parasites.

L16 ANSWER 5 OF 6 MEDLINE on STN DUPLICATE 1
97257080. PubMed ID: 9103750. **Black fly** (Diptera:Simuliidae) salivary secretions: importance in vector competence and disease. **Cupp E W; Cupp M S.** (Department of Entomology, Auburn University, AL 36849-5413, USA.) Journal of medical entomology, (1997 Mar) 34 (2) 87-94. Ref: 76. Journal code: 0375400. ISSN: 0022-2585. Pub. country: United States. Language: English.

AB When blood-feeding, **black flies** introduce secretions into the feeding lesion that act in a coordinated manner on the 3 arms of the vertebrate hemostatic system (platelet aggregation, coagulation, and vasoconstriction). Apyrase activity inhibits platelet aggregation and is ubiquitous in the saliva of **black flies**, although activity per gland varies by species and has a positive association with anthropophagy. Anticoagulants target components in the final common pathway of the coagulation cascade, including factors V, Xa, and II (thrombin). The antithrombin salivary protein may exert a redundant effect by inhibiting the role of thrombin in platelet aggregation. Antithrombin presence and activity also varies among **black fly** species, and exhibits a positive correlation with zoophagy. Vasodilation of capillaries to increase blood supply to the feeding wound appears to be an important requirement for Simulium spp., because substantial erythema-inducing activity, has been demonstrated in salivary glands of all New World species examined. Salivary glands of Simulium ochraceum (Walker), a highly anthropophilic vector of Onchocerca volvulus (Leuckhart), contain greater **vasodilator** activity than several other species, including S. metallicum Bellardi, a secondary zoophagic vector of human onchocerciasis. Simulium vittatum Zetterstedt saliva affects immune cell responses and cytokine production. The ability of the saliva to modulate components of the host immune system provides an opportunity for enhancing transmission of pathogens during bloodfeeding. Thus, the likely possibility that effective pathogen transmission relies on vector saliva may complement present efforts aimed at target epitopes of O. volvulus or identify additional molecules to be investigated as part of a "river blindness" vaccine cocktail. Components in saliva also may enhance the transmission of other microbial agents either by a cofeeding process similar to that observed in ixodid ticks or through rupture of the labrum during escape of Onchocerca infective stage larvae. In a few instances, saliva of some Simulium spp. also has been associated with extensive tissue and organ pathology, including hemorrhagic shock and death. Pathologic signs associated with this syndrome indicate an enhanced antihemostatic activity in saliva.

L16 ANSWER 6 OF 6 MEDLINE on STN DUPLICATE 2
94161217. PubMed ID: 8116819. Vasodilative activity in **black fly** salivary glands. **Cupp M S; Ribeiro J M;**

Cupp E W. (Department of Veterinary Science, University of Arizona, Tucson.) American journal of tropical medicine and hygiene, (1994 Feb) 50 (2) 241-6. Journal code: 0370507. ISSN: 0002-9637. Pub. country: United States. Language: English.

AB Salivary gland extracts of several Simulium spp. were shown to contain vasodilative activity as measured by the rapid and persistent induction of erythema in response to intradermal injection into rabbit skin. Total salivary gland activities were approximately equal for S. vittatum, S. metallicum, S. bivittatum, and S. argus (titers of 0.03-0.02 pairs of gland). Total gland activity in the highly anthropophilic species S. ochraceum, however, was an order of magnitude greater, with erythema produced by as little as 0.002 pairs of glands. Tests for physical stability of the activities from two species (S. vittatum and S. ochraceum) indicated that the **vasodilators** were proteinaceous and heat stable. A two-step, reversed-phase high-performance liquid chromatography (HPLC) procedure was developed that isolated both activities with similar elution patterns. Homogeneity of the purified protein from S. vittatum was confirmed by capillary gel electrophoresis. Electrospray ionization mass spectroscopy of the S. vittatum protein detected a mass of 15,351 daltons. Similarity in elution times of the proteins from a TSK HPLC column predict some structural similarities between the S. vittatum and S. ochraceum **vasodilator** proteins.

=> s l1 and blood pressure

---Logging off of STN---

END

SEARCH ENDED BY USER
L17 19553 L1 AND BLOOD PRESSURE

=>

Executing the logoff script...

ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:LOG Y

LOGOFF? (Y)/N/HOLD:
'LOG Y' IS NOT VALID HERE
For an explanation, enter "HELP LOGOFF".

=> s l17 and therapy
L1 NOT FOUND

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	91.83	92.04

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-6.30	-6.30

STN INTERNATIONAL LOGOFF AT 16:22:38 ON 09 SEP 2004